REMARKS

Claims 10, 13-16, 18, 31, and 33-37 are under prosecution. Claims 1-9, 11-12, 17, 19-30, 32 are canceled. Claims 31 and 36 are amended. Support for the amending language may be found, for example, at page 15, line 19. No new matter is added. Applicants respectfully request reconsideration of the rejections.

The rejection of Claims 38-40 is made moot by the cancellation of the claims.

Claims 10, 13-15, 18, 31, 33-35 and 37 have been rejected under 35 U.S.C. § 103(a) as obvious over Beattie (U.S. Patent No. 5,843,767, filed April 10, 1996) as defined by Zubay. It is stated that Beattie teaches a microarray of discrete polypeptides in a planar solid support. Applicants respectfully submit that the presently claimed invention is not made obvious by the cited combination of references.

The presently pending claims have been amended to recite a microarray on a slide. The use of a slide is shown in the Examples, e.g. on page 22, in the description of array preparation. The term "slide" is known to those of skill in the art as a flat surfaced planar element. One of skill in the art would recognize that a slide cannot exist as a substrate described by Beattie, wherein the substrate comprises (as recited above in Claim 1) "a multiplicity of discrete channels", and where the binding reagent is not on the flat surface but on the walls of the channels, which are curved surfaces. As stated by Beattie, a "variety of materials can be immobilized or fixed to the glass surfaces within the channels of the NCG array, to yield a high surface area to volume ratio[1]", which is not found in a planar surface.

Further, as described in the specification, the invention of Beattie is a "flow-through" sensor, designed "such that said test sample upon contact with said substrate is capable of penetrating therethrough during the course of said binding reaction". It is therefore integral to the Beattie invention that the substrate comprises, not a solid material, but a porous material, and that the substrate not exist as a planar solid such as a slide, but as a microfabricated channeled device.

Beattie specifically teaches away from the use of flat, *i.e.* planar, substrates such as a slide, stating that "Another limitation of these prior art approaches is the fact that a flat surface design introduces a rate-limiting step in the hybridization reaction, i.e., diffusion of target molecules over relatively long distances before encountering the complementary probes on the surface. In contrast, the

[1] column 9, lines 57-59)

microfabricated apparatus according to the present invention is designed to overcome the inherent limitations in current solid phase hybridization materials, eliminating the diffusion-limited step in flat surface hybridizations and increasing the cross sectional density of DNA.[2]"

Applicants respectfully submit the presently claimed invention is not taught or suggested by Beattie.

The teachings of Zubay that an antibody is a polypeptide of at least 50 amino acids is not disputed, however Zubay fails to remedy the deficiencies of Beattie. Zubay in combination with Beattie fail to teach a microarray of discrete polypeptides on a slide, wherein each polypeptide is of at least 50 amino acids in length and wherein said microarray comprises 1000 or more discrete regions of distinct polypeptide per cm^2.

In view of the above amendments and remarks, withdrawal of the rejection is requested.

Claims 10, 13-15, 18, 31, 33-35 and 37-40 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (U.S. Patent no. 4,591,570) as defined by Zubay in view of Beattie. Applicants respectfully submit that the presently claimed invention is not made obvious by the cited combination of references.

Chang *et al.* describes an array of a much lower density than that of the present invention. As set forth in the Chang et al. specification, a 10 spot by 10 spot matrix should occupy about 1 cm^2 of the surface of the support, or to a density of 400 regions per cm^2. These densities are substantially lower than that taught by Applicants and recited in the present claims.

There is no teaching in Beattie or Chang *et al.* that would teach the modification of the low density Chang array to a high density microarray as taught by Applicants. Chang *et al.* utilize a conventional micropipette to spot solutions onto a slide. There is no indication of how one might modify the procedure to provide for a system as taught by Applicants, for example in the use of a reagent dispensing device shown in Figure 1 of the present application.

The teachings of Beattie cannot be combined with the teachings of Chang *et al.*, because Beattie utilizes a microfabricated porous substrate, not a slide. One of skill in the art could not readily adapt the methods of Beattie to the deposition of materials of a non-porous surface, such as a slide. In particular, as discussed above, Beattie teaches away from the use of surface such as a slide, which is said to introduce limitations in the use of the microarray for hybridizations.

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[2] (column 3, lines 18-26)

One of skill in the art would not be motivated by the teachings of Beattie to modify an array such as that taught by Chang *et al.*, in part because it is unclear whether any advantages would be obtained from creating a higher density array on a solid surface such as a slide. Beattie *et al.* teach that the higher cross-sectional surface area obtained with a porous substrate provides advantages, for example by providing a greater surface for binding or hybridization to occur. One of skill in the art may reasonably have expected that these purported advantages are thus relevant to the utility of the Beattie array, and would therefore not have expected such advantages to accrue to a high density array on a slide surface.

In view of the above amendments and remarks, Applicants respectfully submit that the presently claimed invention is not made obvious by the combined references of Chang et al, Beattie and Zubay. Withdrawal of the rejection is requested.

Claims 16 and 36 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang et al., in view of Beattie as defined by Zubay as applied above, and further in view of Van Ness *et al.* The Office Action states that Beattie teaches a microarray comprising binding reagents deposited at defined positions on a planar solid support, but do not teach a cationic film on the solid support. Van Ness et al. specifically teach a cationic film for convenient attachment of polypeptides.

Applicants respectfully submit that the secondary reference does not correct the deficiencies of the primary reference. Van Ness et al. fails to teach or suggest a planar microarray comprising at least 10^3 different polypeptides/cm^2, and there is no suggestion that the methods of polypeptide attachment could be used in the methods as claimed by Applicants.

As demonstrated above, neither Beattie nor Van Ness teach or suggest microarrays on a surface such as a slide, and one of skill in the art is not motivated to combine the teachings of Chang *et al.* and Beattie to provide for a high density array of a solid surface. Applicants respectfully submit the cited combination of references do not make obvious the presently claimed invention. Withdrawal of the rejection is requested.

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-128.

Respectfully submitted,

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